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$\beta^1$  cont (SEQ ID NO: 103) and MBP-C125sw (SEQ ID NO: 104) with (i) a test compound and (ii) a  $\beta$ -secretase substrate, and selecting the test compound as capable of inhibiting A $\beta$  production if said  $\beta$ -secretase polypeptide exhibits less  $\beta$ -secretase activity in the presence of said compound than in the absence of said compound.

$\beta^2$  81. (Amended) The method of claim 78, which further includes administering said test compound to a mammalian subject having a condition characterized by A $\beta$  peptide amyloid deposits, and selecting said compound as a therapeutic agent candidate if, following such administration, said subject maintains or improves cognitive ability or said subject shows reduced plaque burden.

84. (Amended) The method of claim 78, wherein said  $\beta$ -secretase substrate is selected from the group consisting of MBP-C125wt (SEQ ID NO: 103), MBP-C125sw (SEQ ID NO: 104), APP, APPsw, and  $\beta$ -secretase-cleavable fragments thereof.

$\beta^3$  85. (Amended) The method of claim 78, wherein said  $\beta$ -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, and SEQ ID NO: 96.

132. (New) The method of claim 78, wherein the  $\beta$ -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 78, and, SEQ ID NO: 81, and, SEQ ID NO: 97, and selecting the test compound as capable of inhibiting A $\beta$  production if said  $\beta$ -secretase polypeptide exhibits less  $\beta$ -secretase activity in the presence of the test compound than in the absence of the test compound.

$\beta^4$  133. (New) A method of screening for compounds that inhibit A $\beta$  production, comprising contacting an isolated  $\beta$ -secretase comprising a polypeptide that (i) is fewer than about 450 amino acid residues in length, (ii) includes an amino acid sequence that is at least 90% identical to SEQ ID NO: 75 including conservative substitutions thereof, and (iii) exhibits  $\beta$ -

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secretase activity, as evidenced by an ability to cleave a substrate selected from the group consisting of the 695 amino acid isotype of beta amyloid precursor protein ( $\beta$ APP) between amino acids 596 and 597 thereof, MBP-C125wt (SEQ ID NO: 103) and MBP-C125sw (SEQ ID NO: 104) with (i) a test compound and (ii) a  $\beta$ -secretase substrate, wherein the  $\beta$ -secretase substrate is an inhibitor of  $\beta$ -secretase activity.

134. (New) The method of claim 133, wherein the  $\beta$ -secretase substrate has a sequence selected from the group consisting of SEQ ID NO: 72, SEQ ID NO: 78, and, SEQ ID NO: 81, and, SEQ ID NO: 97, and selecting the test compound as capable of inhibiting A $\beta$  production if said  $\beta$ -secretase polypeptide exhibits less  $\beta$ -secretase activity in the presence of the test compound than in the absence of the test compound.

REMARKS

After entry of this amendment, claims 1-134 are pending. Claims 78, 81-85, and 134 are currently under examination. Claims 1-77, 79-80, and 86-131 have been withdrawn from consideration. New claims 132-134 have been added, and claims 78, 81, 84, and 85 have been amended.

As filed, claim 78 recited "an isolated  $\beta$ -secretase according to claim 37." Claim 37 has been withdrawn from consideration, and claim 78 has been amended accordingly. Further support for the amendment to claim 78 is found throughout the specification, *e.g.*, page 19, lines 22-24 and 29-31. Support for the amendment to claim 81 is found throughout the specification, *e.g.*, page 32, lines 17-20; page 50, lines 25-26; and, page 57, lines 2-3. Claim 84 has been amended to include SEQ ID NOS. Support for the amendment to claim 85 is found throughout the specification, *e.g.*, Example 4. The amendments to the claims contain no new matter. Support for new claims 132-134 is found in claims 78 and 85 as originally filed, and throughout the specification, *e.g.*, page 6, lines 1-7 and page 53, lines 1-4.

Election of Species Requirement

Applicants elect MBP-C125sw (SEQ ID NO: 104), SEVNLD AEF (SEQ ID NO: 83), and P10-P4'(D $\rightarrow$ V): KTEEISEVN LV AEF (SEQ ID NO: 97). Claim 84 reads on MBP-C125sw (SEQ ID NO: 104). Claim 85 reads on SEVNLD AEF (SEQ ID NO: 83). Claims 132